Remarks

Support for the Amendments

Support for the amendments to claims 35, 38-41, 52, 69 and 72 and for new claims 101-112 can be found throughout the specification. For example, support for the amendments to claims 35, 39-41, 59 and 72 can be found at page 8, lines 11-20; at page 16, lines 26-31; throughout pages 31-33; and throughout the Examples, particularly Examples 1, 2 and 5. The amendment to claim 38 is made to provide the proper dependency of this claim upon the cancellation of claim 37. Support for new claims 101, 104, 107 and 110 can be found, *inter alia* at page 8, lines 11-20; at page 16, lines 26-31; throughout pages 31-33; and throughout the Examples, particularly, Examples 1, 2 and 5. Support for new claims 102, 103, 105, 106, 108, 109, 111 and 112 can be found at page 13, lines 4-8; throughout pages 18-22; and throughout the Examples. Therefore, these amendments do not add new matter, and their entry and consideration are respectfully requested.

Status of the Claims

By the foregoing amendments, claims 35, 38-41, 52, 69 and 72 are sought to be amended, claims 37, 67, 68, 76 and 78 have been canceled without prejudice or disclaimer and new claims 101-112 are sought to be added. Upon entry of the foregoing amendments, claims 35-36, 38-66, 69-75, 77 and 79-112 are pending in the application, with claims 35, 39, 52, 69 and 72 being the independent claims.

Summary of the Office Action

In the Office Action dated March 25, 2004, the Examiner has made eight rejections of the claims. Based on the following remarks, Applicants respectfully request that the Examiner reconsider all outstanding rejections and that they be withdrawn.

The Rejection Under 35 U.S.C. § 112, First Paragraph

In the Office Action at pages 2-4, the Examiner has rejected claims 52-68 and 87-91 under 35 U.S.C. § 112, first paragraph, alleging that the claims contain subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the art that the inventors, at the time the application was filed, had possession of the claimed invention. Solely to expedite prosecution, and not in acquiescence to this rejection, claims 67 and 68 have been cancelled. Thus, the portion of this rejection that may have applied to these claims has been rendered moot. Applicants respectfully traverse this rejection as it may apply to the remaining claims.

The Examiner contends that the present specification does not provide sufficient basis for the ordinarily skilled artisan to envision embodiments of the claimed invention wherein the nucleic acid encoding a functional antibiotic resistance gene comprises a first portion and a second portion separated by any recombination site sequence. Applicants respectfully disagree with these contentions.

The Examiner's attention is directed to the present specification at page 14, lines 1-15, where several non-limiting examples of recombination sites and recognition sequences are discussed. The Examiner's attention is also directed to page 22, line 15, through page 30, where numerous recombination systems are disclosed, including recombination proteins,

recombination sites, and various mutated recombination sites which may be utilized in the practice of the presently claimed invention. Applicants respectfully submit that the ordinarily skilled artisan would readily recognize that any of these recombination sites and systems can be successfully utilized in the practice of the presently claimed invention. The Examiner has provided no evidence that would indicate that exchanging the various recombination sites discussed in the present specification for the recombination sites utilized in the Examples would in any way alter or preclude the practice of the presently claimed invention.

Furthermore, Applicants submit that the numerous examples utilizing various recombination sites and systems provide the ordinarily skilled artisan with a sufficient basis to envision the breadth of the present claims. The Examiner's attention is directed to page 19, lines 9-24 describing Figure 2; to Example 2 at page 36 describing Figures 4A-4C; and to Example 5, all of which provide non-limiting examples of nucleic acid molecules within the scope of the present invention comprising various *att* and *lox* sites. The ordinarily skilled artisan would readily recognize that any of the various recombination sites, including mutated recombination sites, disclosed throughout the present specification may be exchanged for one another in the practice of the presently claimed invention. Applicants submit that there is no reason provided by the Examiner, or otherwise, for the ordinarily skilled artisan to believe that the presently claimed invention could not be practiced using any of the numerous recombination sites disclosed throughout the present specification and others that are well-known in the relevant art.

Applicants wish to remind the Examiner that "[a]dequate description under the first paragraph of 35 U.S.C. 112 does not require literal support for the claimed invention . . . the

observation of a lack of literal support does not, in and of itself, establish a *prima facie* case for lack of adequate descriptive support under the first paragraph of 35 U.S.C. 112." *Ex parte Parks*, 30 USPQ2d 1234, 1236 (Bd. Pat. App. Int. 1994). Instead, the written description requirement of 35 U.S.C. § 112, first paragraph, is met "if the originally-filed disclosure would have conveyed to one having ordinary skill in the art that an [applicant] had possession of the concept of what is claimed," *id.*, *i.e.*, "[i]f a person of ordinary skill in the art would have understood the inventor to have been in possession of the claimed invention at the time of filing, even if every nuance of the claims is not explicitly described in the specification . . . ." *In re Alton*, 37 USPQ2d 1578, 1584 (Fed. Cir. 1996). An applicant is not required to disclose or provide a working example of every species of a given genus in order to meet the written description requirement of 35 U.S.C. § 112 (*see Parks and Alton*), and subject matter that "might fairly be deduced from the original application" is considered to be described in the application as filed. *Acme Highway Products Corp. v. D.S. Brown Co.*, 431 F.2d 1074, 1080 (6th Cir. 1970) (citations omitted), *cert. denied*, 401 U.S. 956 (1971), *followed by Westphal v. Fawzi*, 666 F.2d 575, 577 (C.C.P.A. 1981). Moreover:

> [a] description of a genus of [nucleic acid molecules] may be achieved by means of a recitation of a representative number of [nucleic acid molecules], defined by nucleotide sequence, falling within the scope of the genus . . . .

Regents of Univ. of Calif. v. Eli Lilly & Co., 119 F.3d 1559, 1569 (Fed. Cir. 1997).

As noted above, the present specification describes a number of representative examples of the claimed genus of recombination sites, and provides detailed specifications for the physical and/or structural characteristics of other nucleic acid molecules that would

fall within the scope of claims 52-68 and 87-91. In so doing, the "representative number" standard under *Eli Lilly*, upon which the Written Description Guidelines (M.P.E.P. § 2163) are based, is clearly met by the present specification. Hence, Applicants respectfully assert that the present specification provides sufficient written description to convey to one of ordinary skill that Applicants had possession of the full scope of the claimed invention upon filing of the application.

In view of the foregoing remarks, Applicants respectfully submit that the ordinarily skilled artisan would readily recognize that Applicants were in full possession of the claimed invention at the time the application was filed. Applicants respectfully request that the rejection of claims 52-68 and 87-91 under 35 U.S.C. § 112, first paragraph, be reconsidered and withdrawn.

The Rejections Under 35 U.S.C. § 112, Second Paragraph

In the Office Action at pages 4-5, the Examiner has rejected claims 39-68 and 79-96 under 35 U.S.C. § 112, second paragraph, for various reasons. Solely to expedite prosecution, and not in acquiescence to these rejections, claims 67 and 68 have been cancelled. Thus, the portion of these rejections that may have applied to these claims have been rendered moot. Applicants respectfully traverse these rejections as they may apply to the remaining claims as follows.

The Examiner has first rejected claims 39, 43-45, 52, 55-56 and 58-60 under 35 U.S.C. § 112, second paragraph alleging that that term "recombination site" is vague and indefinite. Applicants respectfully disagree. As the Examiner has correctly noted, the ordinarily skilled artisan, upon reading the present specification, would readily understand

that the term "recombination site" refers to a site-specific recombination site. Applicants submit that the term "recombination site" was well known in the art at the time of the filing of the present application to mean a site-specific recombination site. The Examiner's attention is also directed to the present specification at page 17, lines 1-10, where site-specific recombination is defined and distinguished from homologous recombination and transposition; and to page 18, lines 19-20, and page 19, lines 23-14, where non-limiting examples of recombination sites, *e.g.*, the site-specific recombination sites *att* and *lox*, are discussed. Other recombination sites and their corresponding recombination proteins are also disclosed in the present specification, *e.g.*, at pages 24-26. Finally, the term "recombination site" is used in this context and with this meaning consistently throughout the present specification (*see, e.g.*, p. 26, line 16 though page 30). Hence, one of ordinary skill in the art would readily understand the meaning of the term "recombination site" as it is used in the present claims.

The Examiner also asserts that the dependent claims drawn to nucleic acids comprising specific site-specific recombination sequences (e.g., *lox*P) are vague and indefinite, because such nucleic acids may contain sequences at the recombination site in addition to the site-specific sequence. Applicants respectfully disagree with this assertion. Applicants submit that the ordinarily skilled artisan would readily understand that indeed, the nucleic acid molecules of the present invention can comprise, and often will comprise, nucleotide sequences at the recombination site in addition to the site-specific recombination sequences. However, Applicants respectfully submit that this fact does not render the recitation of "recombination site" vague or indefinite, as the ordinarily skilled artisan would readily understand the meaning of this term as it is used in the present specification and

claims, regardless of whether or not additional nucleotide sequences are also located at or near the recombination site on a given nucleic acid molecule. Further, the ordinarily skilled artisan would readily understand that nucleic acid molecules comprising such site-specific recombination sites may also comprise additional sequences, so long as the recited site-specific recombination site(s) is (are) present and capable of functioning as desired.

In view of the foregoing remarks, Applicants respectfully request that the rejection of claims 39, 43-45, 52, 55-56 and 58-60 under 35 U.S.C. § 112, second paragraph, be reconsidered and withdrawn.

The Examiner has next rejected claim 40 under 35 U.S.C. § 112, second paragraph, stating that there is insufficient antecedent basis for the term "first" in the phrase "said first recombination site." In view of the foregoing amendment to claim 40 to recite "said at least one recombination site," this rejection has been fully accommodated. Therefore, Applicants respectfully request reconsideration and withdrawal of this rejection.

The Examiner has also rejected claims 47 and 62 under 35 U.S.C. § 112, second paragraph, alleging that the term "cloning site" is vague and indefinite, as it is unclear what the term encompasses. Applicants respectfully disagree with this allegation.

Applicants respectfully submit that the ordinarily skilled artisan would readily understand that the term "cloning site" encompasses any site within a given nucleic acid molecule which allows for insertion of a desired sequence. The Examiner's attention is drawn to the present specification at page 32, line 27 through page 33, line 2, where the vector pEZC602 shown in Figure 3D is described. The vector pEZC602 comprises "*lox*P and *lox*P511 sites flanking a multiple cloning site." Referring then to Figure 3D, the positions of the *lox*P and *lox*P511 sites and the multiple cloning site region between the two

sites are clearly shown. Applicants submit that the term "cloning site" is therefore sufficiently defined in the present specification and would be readily understood by the ordinarily skilled artisan. In view of the foregoing remarks, Applicants respectfully request reconsideration and withdrawal of the rejection of claims 47 and 62 under 35 U.S.C. § 112, second paragraph.

Finally, the Examiner has rejected claims 67 and 68 under 35 U.S.C. § 112, second paragraph, alleging that the term "adjacent" is vague and indefinite. Applicants respectfully traverse this rejection. However, solely to expedite prosecution, and not in acquiescence to this rejection, claims 67 and 68 have been cancelled. Thus, this rejection has been rendered moot.

The Rejection Under 35 U.S.C. § 102(b) Over Dale

In the Office Action at pages 5-6, the Examiner has rejected claims 35-50, 69-70, 72-73, 75-87 and 98-100 under 35 U.S.C. § 102(b), as being anticipated by Dale and Ow, *Proc. Natl. Acad. Sci. 88*:10558-10562 (1991) (Document AS14 of record; hereinafter "Dale"). Solely to expedite prosecution, and not in acquiescence to this rejection, claims 37, 76 and 78 have been cancelled. Thus, the portion of this rejection that may have applied to these claims has been rendered moot. Applicants respectfully traverse this rejection as it may apply to the remaining claims.

Applicants respectfully submit that the rejection of claim 87 has been made in error, as the Examiner has not rejected claim 52 from which claim 87 ultimately depends. In view of this fact, Applicants presume that the Examiner has concluded that present claim 52 is patentable over Dale. Hence, Applicants respectfully submit that dependent claim 87 also is

patentable over Dale. Reconsideration and withdrawal of the rejection of claim 87 is therefore respectfully requested.

The Examiner states that Dale discloses a nucleic acid molecule comprising a *lox*P site separating a promoter (35s) and an ampicillin resistance gene, where the promoter and resistance gene are operably linked, and concludes therefore that Dale discloses the presently claimed invention. Applicants respectfully disagree with this conclusion and offer the following remarks with respect to each independent claim to overcome this rejection.

Present claim 35 (and hence claims 36, 38, 75 and 77 that depend ultimately therefrom and that are also rejected over Dale) recites a nucleic acid molecule comprising at least a first *lox* site located immediately adjacent to at least one promoter, wherein the promoter is operably linked to at least one antibiotic resistance gene.

Applicants respectfully submit that Dale does not disclose a nucleic acid molecule comprising at least a first *lox* site located immediately adjacent to at least one promoter which is operably linked to at least one antibiotic resistance gene. Instead the nucleic acid molecule disclosed in Dale (Page 10559, Figure 1) comprises a *lox* site that is not immediately adjacent to the promoter operably linked to the ampicillin resistance gene. As one of ordinary skill would readily understand, the 35S promoter and the lox site in this figure in Dale are separated by intervening nucleotides, as evidenced by the presence of the luc and nos3′ genes shown in Figure 1.

Under 35 U.S.C. § 102, a claim can only be anticipated if every element in the claim is expressly or inherently disclosed in a single prior art reference. *See Kalman v. Kimberly Clark Corp.*, 713 F.2d 760, 771 (Fed. Cir. 1983), *cert. denied*, 465 U.S. 1026 (1984). Applicants respectfully submit that Dale does not disclose every element of claim 35 (and

thus the dependent claims noted above), and therefore cannot anticipate the claimed invention.

Present claim 39 (and hence claims 40-50 and 79-86 that depend ultimately therefrom and that are also rejected over Dale) recites a nucleic acid molecule comprising at least one promoter operably linked to at least one antibiotic resistance gene, wherein the promoter and the antibiotic resistance gene are separated by at least one recombination site, and wherein the promoter or the antibiotic resistance gene is immediately adjacent to the at least one recombination site. In contrast, Dale does not disclose a nucleic acid molecule which comprises at least one promoter and at least one antibiotic resistance gene which are separated by, at least one recombination site, wherein either the promoter or the antibiotic resistance gene are immediately adjacent to a recombination site. As noted above, the 35S promoter in Dale is separated from the *lox* site by both the luc and the nos3′ genes. Furthermore, in Dale, the ampicillin resistance gene is separated from the *lox* site by several nucleotides, as evidenced by both Figure 2A and Figure 3 in that reference. The top nucleic acid sequence shown in Figure 3 (A+B) of Dale shows that there are multiple intervening nucleotides flanking both sides of the *lox* site. Hence, in Dale, *neither* the 35S promoter *nor* the ampicillin antibiotic resistance gene are immediately adjacent to the *lox* site. In view of the foregoing remarks, Applicants respectfully submit that Dale does not disclose every element of, and therefore cannot anticipate, claim 39 (and hence the dependent claims noted above).

Present claim 69 (and hence claims 70 and 98 that depend ultimately therefrom and that are also rejected over Dale) recites a nucleic acid molecule comprising at least one promoter operably linked to at least one antibiotic resistance gene, wherein the promoter and

the antibiotic resistance gene are separated by at least one *lox*P site, and wherein the promoter or the antibiotic resistance gene is immediately adjacent to the at least one *lox*P site.

Present claim 72 (and hence claims 73, 99 and 100 that depend ultimately therefrom and that are also rejected over Dale) recites a nucleic acid molecule comprising at least one functional antibiotic resistance gene, wherein the functional gene comprises a promoter and an antibiotic resistance gene separated from each other by at least one *lox*P site, and wherein the promoter or the antibiotic resistance gene is immediately adjacent to the at least one *lox*P site.

With respect to claims 69 and 72, as noted above, Applicants respectfully submit that Dale does not disclose a nucleic acid molecule which comprises at least one promoter and at least one antibiotic resistance gene (or functional antibiotic resistance gene) in which either the promoter or the at least one antibiotic resistance gene is also immediately adjacent to at least one recombination site (e.g., *lox*P). Applicants further submit that the nucleic acid molecules disclosed in Dale do not comprise the *lox*P recombination site as the Examiner contends. Applicants note that the nucleic acid sequence shown in Figure 3 on page 10560, and identified by the Examiner's notation as *lox*P, is a *lox* site, but is not the *lox*P sequence. Applicants respectfully submit that the 8 base-pair core region of the *lox* sequence shown in Figure 3 does not match the 8 base-pair core region of *lox*P. (*See Wang, C.L., et al., Retrovirology 1*:5 (2004), at page 12, second full paragraph, attached hereto as Exhibit A.) Hence, Applicants respectfully submit that Dale does not disclose every element of, and therefore cannot anticipate, claims 69 and 72 (and hence the dependent claims noted above).

In view of the foregoing arguments, and in view of *Kalman*, Applicants respectfully submit that Dale does not disclose every element of, and therefore does not anticipate, the presently claimed invention. Reconsideration and withdrawal of the rejection of claims 35-36, 38-50, 69-70, 72-73, 75, 77, 79-87 and 98-100 under 35 U.S.C. § 102(b) over Dale therefore are respectfully requested.

The Rejection Under 35 U.S.C. § 102(b) Over Palazzolo

In the Office Action at pages 6-7, the Examiner has rejected claims 35-50, 52-65, 67-70, 72-73 and 75-100 under 35 U.S.C. § 102(b), as being anticipated by Palazzolo *et al.*, *Gene 88*:25-36 (1990) (hereinafter "Palazzolo"). Applicants respectfully traverse this rejection. However, solely to expedite prosecution, and not in acquiescence to this rejection, claims 37, 67, 68, 76 and 78 have been cancelled. Thus, the portion of this rejection that may have applied to these claims has been rendered moot. Applicants respectfully traverse this rejection as it may apply to the remaining claims.

The Examiner contends that Palazzolo discloses a nucleic acid molecule comprising an SP6 promoter operatively linked to an antibiotic resistance gene, where the promoter and the antibiotic resistance gene are separated by a *lox*P site, and therefore concludes that Palazzolo discloses the present invention. Applicants respectfully disagree with these contentions and conclusions.

As noted above, present claim 35 (and hence claims 36, 38, 75 and 77 that depend ultimately therefore and that are also rejected over Palazzolo) recites a nucleic acid molecule comprising at least a first *lox* site located immediately adjacent to at least one promoter, wherein the promoter is operably linked to at least one antibiotic resistance gene. Applicants

respectfully submit that Palazzolo does not disclose a nucleic acid molecule comprising a *lox* site immediately adjacent to a promoter that is operably linked to an antibiotic resistance gene.

The Examiner's attention is directed to Palazzolo at page 30, Figure 4. The Examiner has made a notation on Figure 4 of the copy of Palazzolo provided to Applicants, indicating that the bla gene is located to the left of the T7 promoter in the linearized nucleic acid molecule, λEXLX±. Applicants respectfully submit that the Examiner is incorrect in this belief. The legend accompanying Figure 4 describes the digestion of plasmid pMP3(±) with *Sma*I and subsequent insertion into the λLOX vector arms shown in Figure 2. Digestion of plasmid pMP3(±) generates a linear nucleic acid molecule, cut at the *Sma*I site on the plasmid. Insertion into the λLOX vector arms add one *lox*P site at either end of the linear nucleic acid molecule as shown at the bottom of Figure 4. The entire pMP3(±) plasmid must therefore be contained between the two *lox*P sites (indicated by bold section of line in the linear molecule at the bottom of Figure 4). Applicants respectfully submit that the bla gene therefore must also be contained within the linear molecule, and in fact would be located to the right of the SP6 promoter and to the left the *lox*P site located to the far right of the linear molecule. Applicants therefore respectfully submit that in the molecule depicted in Figure 4 of Palazzolo, the bla gene cannot be located to the left of the T7 promoter as indicated in the Examiner's notation on page 30.

The Examiner's attention is also directed to Palazzolo at page 32, Figure 6A, showing a vector map of the circularized pEXLX(+) vector. This vector is produced following *in vivo* Cre-catalyzed recombination between the two *lox*P sites on the linear λEXLX± molecule shown at the bottom of Figure 4 (See Palazzolo, Figure 6, line 1; page 28, second

column, paragraph (ii)). The recombination generates the circular pEXLX(+) vector comprising one *lox*P site and the rest of the vector as shown. Applicants note that the bla gene is under the control of the T7 promoter in both the linearized molecule in Figure 4 and the circularized vector in Figure 6. However, the SP6 promoter in both Figure 4 and Figure 6 is *not* operably linked to the bla gene as evidenced by the opposite orientation of the SP6 promoter from the transcriptional direction of the bla gene in these figures in Palazzolo.

Hence, Applicants respectfully submit that in the nucleic acid molecules disclosed in Palazzolo, the *lox*P site is not immediately adjacent to the T7 promoter that is operably linked to the bla gene. It is evident from both Figure 4 and Figure 6 in Palazzolo that there are intervening nucleotides between the *lox*P site and the T7 promoter. Thus, Applicants respectfully submit that Palazzolo does not disclose every element of the present claims, and therefore, under *Kalman*, cannot and does not anticipate the presently claimed invention.

Present claim 39 (and hence claims 40-50 and 79-86 that depend ultimately therefrom and that are also rejected over Palazzolo) recites a nucleic acid molecule comprising at least one promoter operably linked to at least one antibiotic resistance gene, wherein the promoter and the antibiotic resistance gene are separated by at least one recombination site, and the promoter or the antibiotic resistance gene is immediately adjacent to the at least one recombination site. Similarly, present claim 69 (and hence claims 70, 97 and 98 that depend ultimately therefrom and that are also rejected over Palazzolo) recites a nucleic acid molecule comprising at least one promoter operably linked to at least one antibiotic resistance gene, wherein the promoter and the antibiotic resistance gene are separated by at least one *lox*P site, and the promoter or the antibiotic resistance gene is immediately adjacent to the at least one *lox*P site.

Applicants respectfully submit that Palazzolo does not disclose a nucleic acid molecule comprising a promoter and an antibiotic resistance gene separated by a recombination site (or a *lox*P site), wherein either the promoter or the antibiotic resistance gene is immediately adjacent to the recombination site (or a *lox*P site), and the promoter and the antibiotic resistance gene are operably linked. As noted above, the bla antibiotic resistance gene shown in both Figure 4 and Figure 6A of Palazzolo is operably linked to the T7 promoter. In the linear nucleic acid molecule shown in Figure 4, and in the circularized vector shown in Figure 6A, neither the T7 promoter nor the bla gene is immediately adjacent to the recombination site (*lox*P) that separates the promoter and the bla gene. In fact, in the linear nucleic acid molecule shown in Palzollo in Figure 4, the T7 promoter and the bla gene are not separated by a recombination site at all, as both of the *lox*P sites are outside of the portion of the vector comprising the T7 promoter and the bla gene. As noted above, in these figures in Palazzolo, the T7 promoter clearly is not immediately adjacent to the *lox*P site. Furthermore, the bla gene is separated from the *lox*P site by the pUC origin of replication (pUC ori) shown in Figure 6A in this reference. Clearly there would be intervening nucleotides between the *lox*P site and the bla gene, and hence the *lox*P and the bla gene are not immediately adjacent to each other. In view of these remarks, Applicants respectfully submit that Palazzolo does not disclose every element of the present claims.

Present claim 52 (and hence claims 53-65 and 87-96 that depend ultimately therefrom and that are also rejected over Palazzolo) recites a nucleic acid molecule comprising a functional antibiotic resistance gene, wherein a first portion of the antibiotic resistance gene and a second portion of the antibiotic resistance gene are separated by at least a first recombination site, wherein the first portion of the antibiotic resistance or the

second portion of the antibiotic resistance gene is immediately adjacent to the first recombination site.

Similarly, present claim 72 (and hence claims 73, 99 and 100 that depend ultimately therefrom and that are also rejected over Palazzolo) recites a nucleic acid molecule comprising at least one functional antibiotic resistance gene, wherein the functional gene comprises a promoter and an antibiotic resistance gene separated from each other by at least one *lox*P site, and the promoter or the antibiotic resistance gene is immediately adjacent to the at least one *lox*P site.

Applicants respectfully submit that the nucleic acid molecules disclosed in Palazzolo do not disclose a functional antibiotic resistance gene comprising a first portion (*e.g.*, a promoter) and a second portion (*e.g.*, the coding sequence of an antibiotic resistance gene) separated by at least one recombination site (*e.g.*, loxP), where the first portion or the second portion of the gene is immediately adjacent to the recombination site. As noted above, in the nucleic acid molecule disclosed in Palazzolo in Figure 4, a first portion of an antibiotic resistance gene (*e.g.*, a T7 promoter) is not separated from a second portion (*e.g.*, a bla gene) by a recombination site. Furthermore, the nucleic acid molecule comprising the functional antibiotic resistance gene disclosed Palazzolo in Figure 6 (bla under the control of the T7 promoter) does not comprise either a first portion or a second portion of the antibiotic resistance gene that is immediately adjacent to the recombination site that separates the two portions. Therefore, Applicants respectfully submit that Palazzolo does not disclose all of the elements of the present claims, and therefore cannot anticipate the presently claimed invention.

In view of the foregoing remarks, Applicants respectfully submit that Palazzolo does not disclose every element of the presently claimed invention. Hence, in view of *Kalman*, Palazzolo cannot and does not anticipate the present invention. Reconsideration and withdrawal of the rejection of claims 35-50, 52-65, 67-70, 72-73 and 75-100 under 35 U.S.C. § 102(b) over Palazzolo are respectfully requested.

The Rejection Under 35 U.S.C. § 103(a) Over Palazzolo and Lenski

In the Office Action at pages 7-9, the Examiner has rejected claims 51, 66, 71 and 74 under 35 U.S.C. § 103(a), as being unpatentable over Palazzolo in view of Lenski *et al.*, *J. Bacteriol. 176*:3140-3147 (1994) (hereinafter "Lenski"). Applicants respectfully traverse this rejection.

The Examiner contends that Palazzolo discloses all limitations of the presently claimed invention, except for the use of the antibiotic resistance gene chloramphenicol. The Examiner relies on the disclosure of Lenski to cure this deficiency. Applicants respectfully disagree with this contention.

As discussed above, Palazzolo does not disclose the nucleic acid molecules of the present invention, and therefore Palazzolo cannot support a *prima facie* case of obviousness. The deficiencies in Palazzolo are not cured by the disclosure of Lenski, as Lenski does not disclose or suggest nucleic acid molecules comprising recombination sites at all, much less in the orientations and relationships with regard to antibiotic resistance genes (or portions thereof) or promoters as required in the presently claimed invention. Therefore, Palazzolo and Lenski, alone or in combination, do not disclose or suggest the presently claimed invention.

Furthermore, Applicants respectfully submit that the ordinarily skilled artisan would have found no motivation in the disclosures of Palazzolo or Lenski to combine these two references. The ordinarily skilled artisan reading the disclosure of Palazzolo would not have been motivated to seek out additional antibiotic resistance genes beyond those disclosed. Furthermore, even assuming *arguendo* that such motivation did exist, the skilled artisan would not have looked to the disclosure of Lenski for such additional antibiotic resistance genes, as the disclosure of Lenski provides no indication of the use of these antibiotic resistance genes in combination with nucleic acid molecules that comprise recombination sites.

In view of the forgoing remarks, Applicants submit that Palazzolo, in view of Lenski, cannot support a *prima facie* case of obviousness. Applicants therefore respectfully request that the rejection of claims 51, 66, 71 and 74 under 35 U.S.C. § 103(a) be reconsidered and withdrawn.

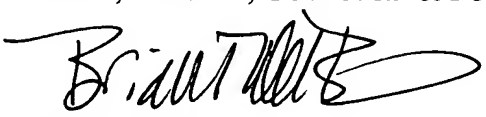
Conclusion

All of the stated grounds of rejection have been properly traversed, accommodated, rendered moot or otherwise overcome. Applicants therefore respectfully request that the Examiner reconsider all presently outstanding rejections and that they be withdrawn.

Applicants believe that a full and complete reply has been made to the outstanding Office Action and, as such, the present application is in condition for allowance. If the Examiner believes, for any reason, that personal communication will expedite prosecution of this application, the Examiner is invited to telephone the undersigned at the number provided.

Respectfully submitted,

STERNE, KESSLER, GOLDSTEIN & FOX P.L.L.C.



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